PPCM and Cardiogenic Shock

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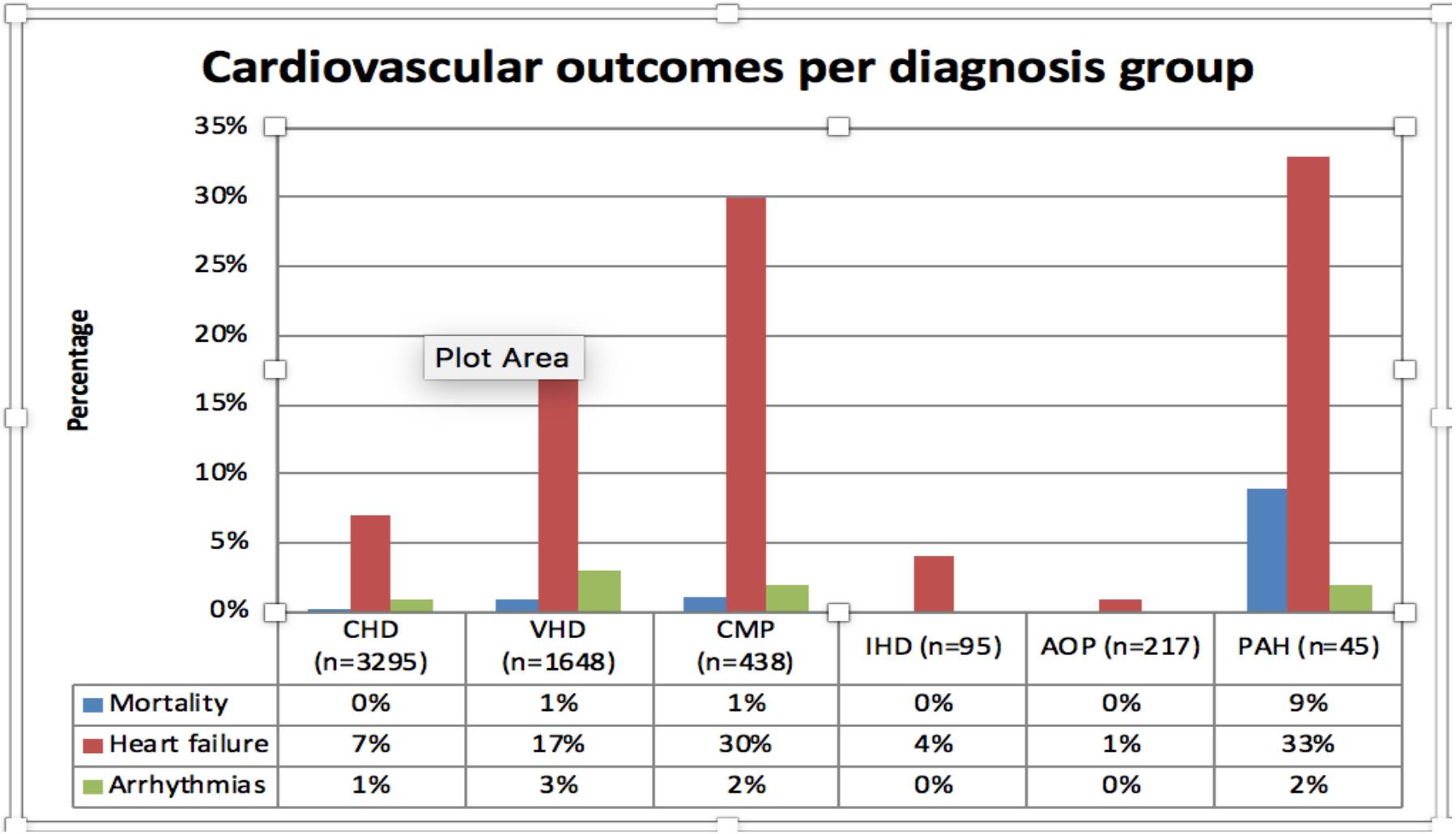
CV Outcome Per Diagnosi

Registry of Pregnancy and Cardiac Disease (ROPAC)

Roos-Heselink et al. Eur Heart J 2019;Feb 25



	CHD (n=3295)	VHD (n=1648)	CMP (n=438)	IHD (n=95)	AOP (n=217)	PAH (n=45)
Mortality	0%	1%	1%	0%	0%	9%
Heart failure	7%	17%	30%	4%	1%	33%
Arrhythmias	1%	3%	2%	0%	0%	2%

Changes in Plasma Volume During Pregnancy

Pitkin RM *Clin Obstet Gyn* 1976;19:489

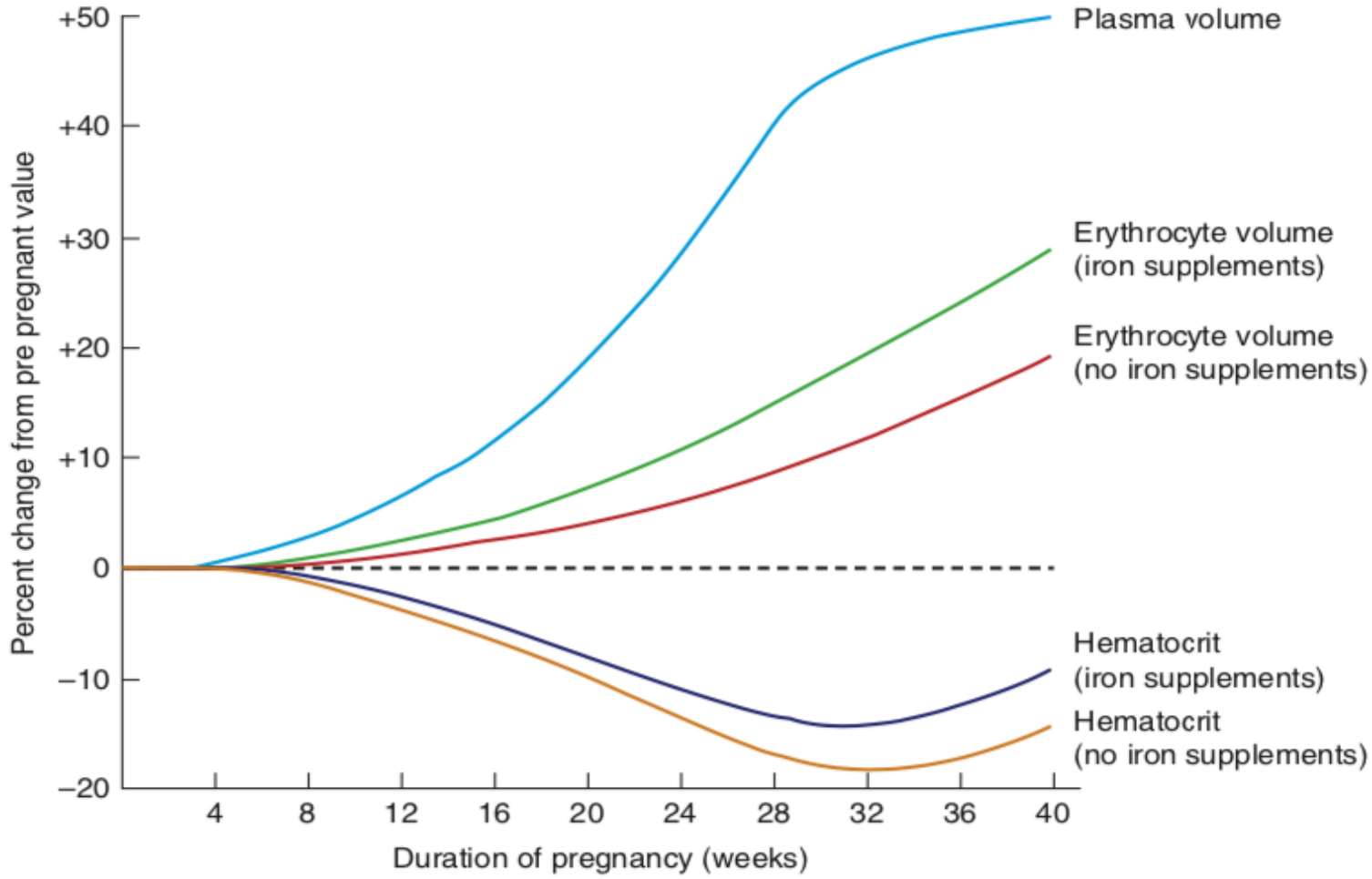
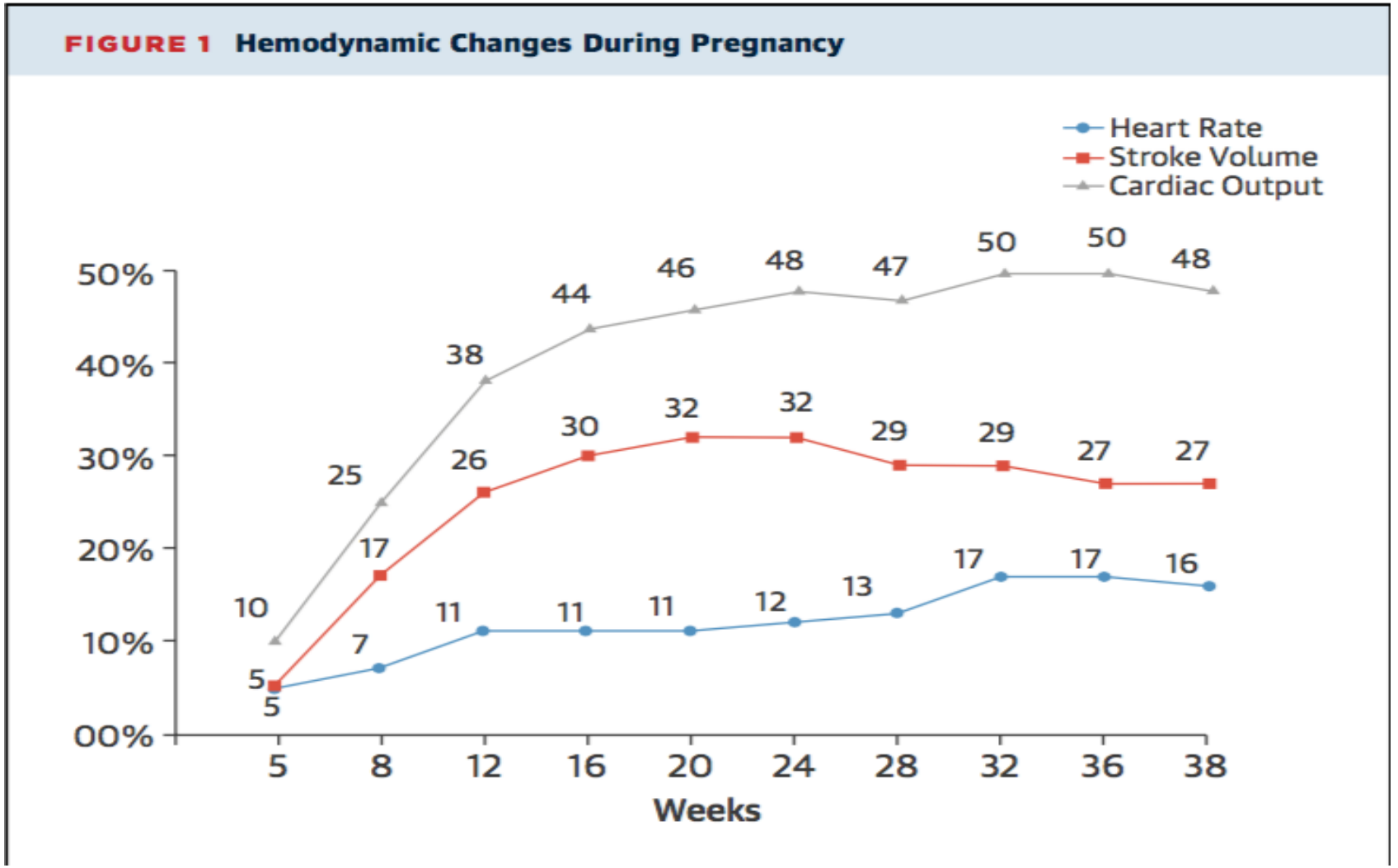


Figure 1.1 Changes in plasma volume, erythrocyte volume, and hematocrit during pregnancy. Increase in plasma volume is more rapid than the increase in erythrocyte volume, causing the "physiological anemia of pregnancy." Source: Pitkin 1976 [41]. Reproduced with permission of Wolters Kluwer Health, Inc.

Hemodynamic Changes During Pregnancy

Elkayam U et al JACC 2016;26:396-410



1998 and Robson et al 1979

Hemodynamic changes during labor and delivery

- Uterine contractions are associated with a significant increase in blood volume but also increase in SVR due to obstruction of the aorta and iliac arteries.
- Valsalva is associated with an increase in PCW pressure and BP.
- Epidural anesthesia is associated with reduction in SVR and BP.
- General anesthesia may result in myocardial depression and intubation with increase in BP and increase LV filling pressure.
- A C section can result in a significant blood loss.

Effect of Maternal Posture

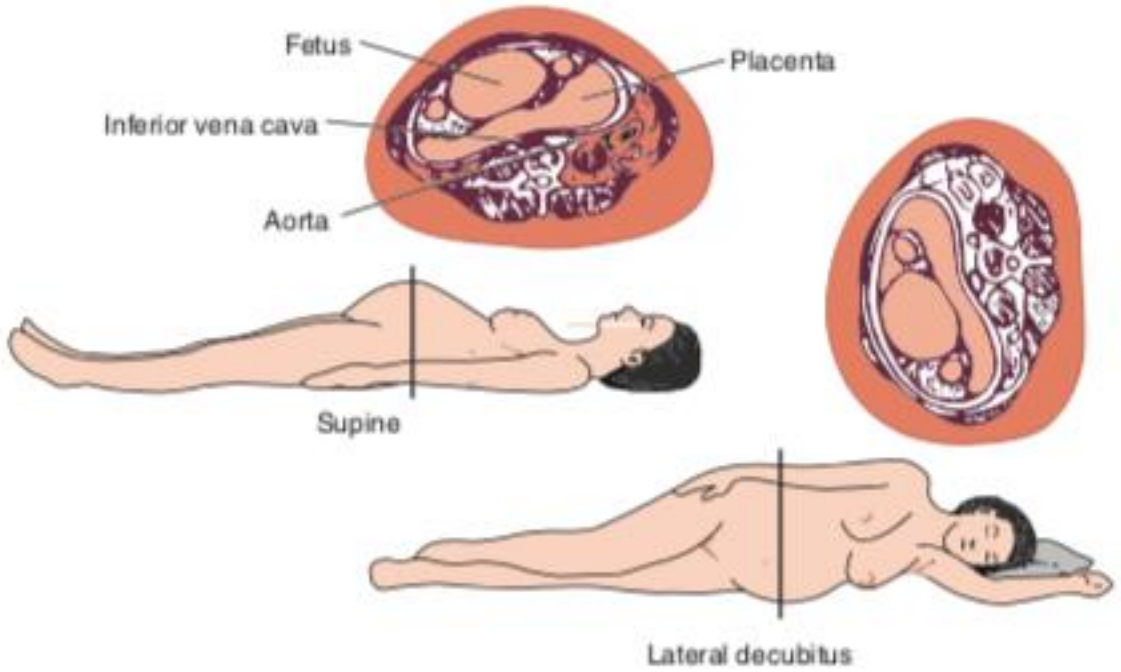


Figure 1.3 After about 20 weeks of gestation, vasocaval compression of the inferior vena cava can lead to reduced venous return and thus to decreased cardiac output and blood pressure.

Hemodynamic changes after the delivery.

- CO may increase by as much as 50% as a result of an auto-trnasfusion from the contracting uterus and increased venous return due to relief of caval compression.
- Increase in SVR.

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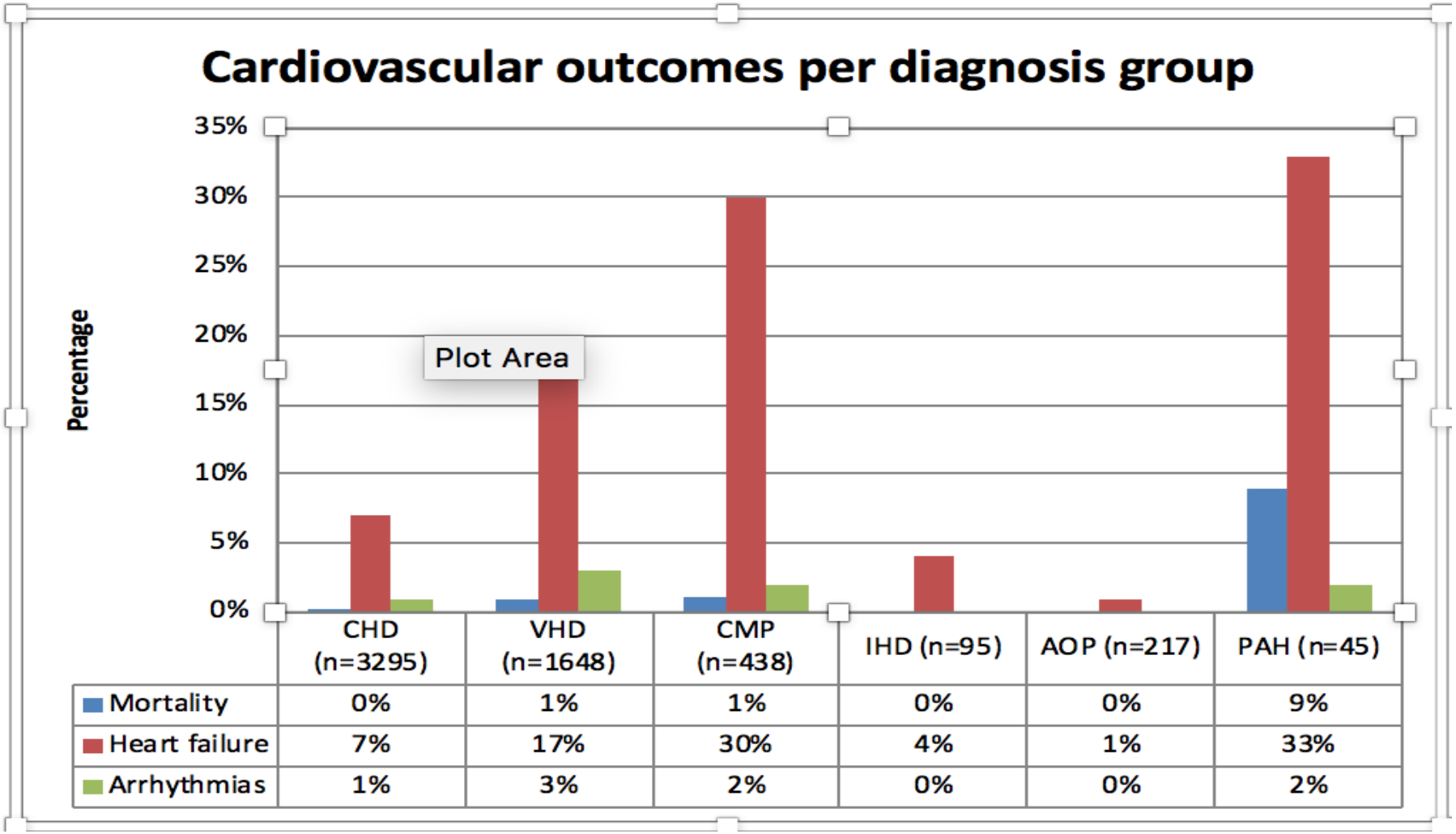

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Arrhythmias	1%	3%	2%	0%	0%	2%

Methamphetamine Induced Cardiomyopathy

- Dilated cardiomyopathy.
- Characterized by severe LV dilatation and reduced ejection fraction.
- High incidence of intra cardiac thrombi.
- Can be reversible with discontinuation of methamphetamine use.
- Presenting with severe symptoms in the 2^{nd}/3^{rd} trimester.

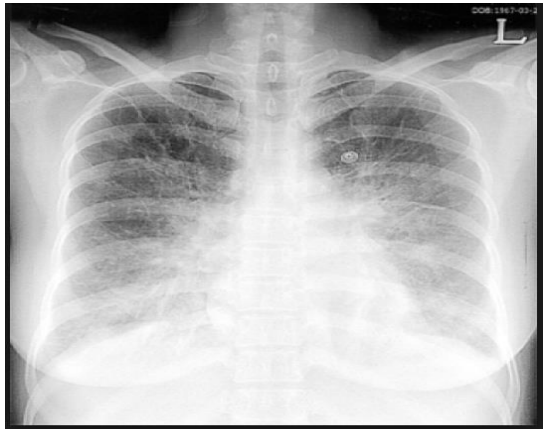
Methamphetamine Induced Cardiomyopathy

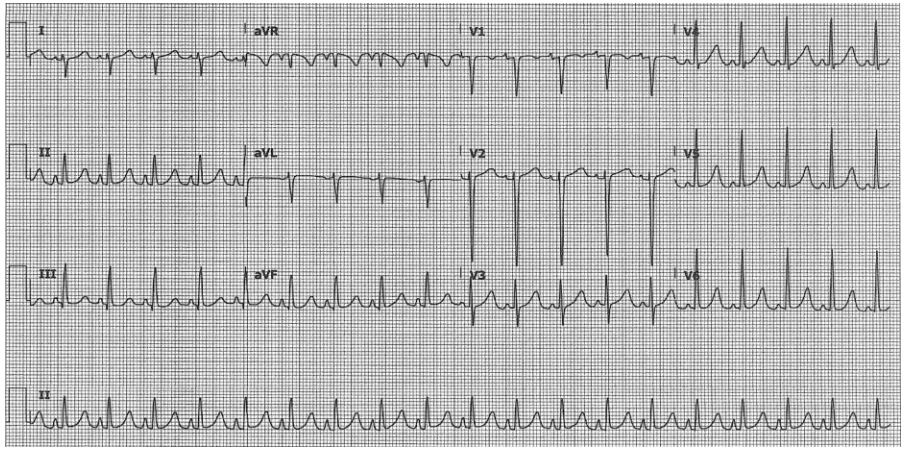
A 29 y/o Hispanic F, G4P3, 33+5 weeks. Referred to our program with complaints of increasing shortness of breath.

- Methamphetamine abuse – 4 years, until 3 months ago.
- No functional limitations prior to pregnancy.
- 3 normal previous pregnancies and deliveries. CS x 3.
- No home medications.

Methamphetamine Induced Cardiomyopathy

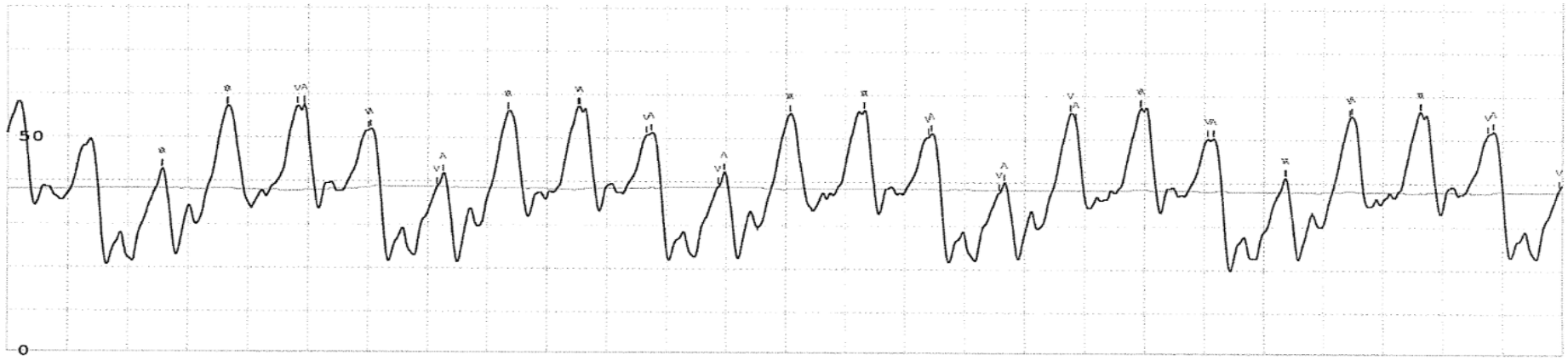
- Symptoms began 1 month ago and progressed.
- NYHA class III-VI on presentation.
- BP 98/65, HR 110 regular, RA sat 91%
- Volume overload.





Methamphetamine Induced Cardiomyopathy

- **CTA** – no evidence of PE; signs of congestion.
- **Echo** – EF 25%, enlarged LV, normal RV, moderate MR, SPAP 42 mmHg.
- **RHC** – RA 13, RV 60/12, PA 59/36, PCWP 35



Management of Severe HF During Pregnancy

- Timing and mode of delivery.
- Can the patient be stabilized?
- Patient wish.
- Safety and efficacy of aggressive management of severe heart failure in pregnancy.
- Hemodynamic monitoring.

Methamphetamine Induced Cardiomyopathy

- Managed with high dose IV Furosemide, IV NTG, PO ISDN+ Hydralazine, small dose metoprolol, IV Heparin.
- Delivered by C section at 35+3 weeks under hemodynamic monitoring.
- Epidural anesthesia.

Too Early for PPCM?

- We have a 30 yo F at 26 w gestation with multi focal VT, LVEF 15-20%, severe MR , BNP 1200 . Improved on esmolol and lidocaine
- Possible viral syndrome (mild) at the beginning of pregnancy, No febrile disease throughout.
- HF service recommended steroid treatment.

Additional Questions

- Since 26 weeks is kind of early for PPCM I wanted your opinion on making such a diagnosis.
- Where do we stand today with bromocriptine?
- How do you manage severe heart failure/cardiogenic shock in patient with PPCM presenting during pregnancy.
- Timing and mode of delivery and anesthesia.

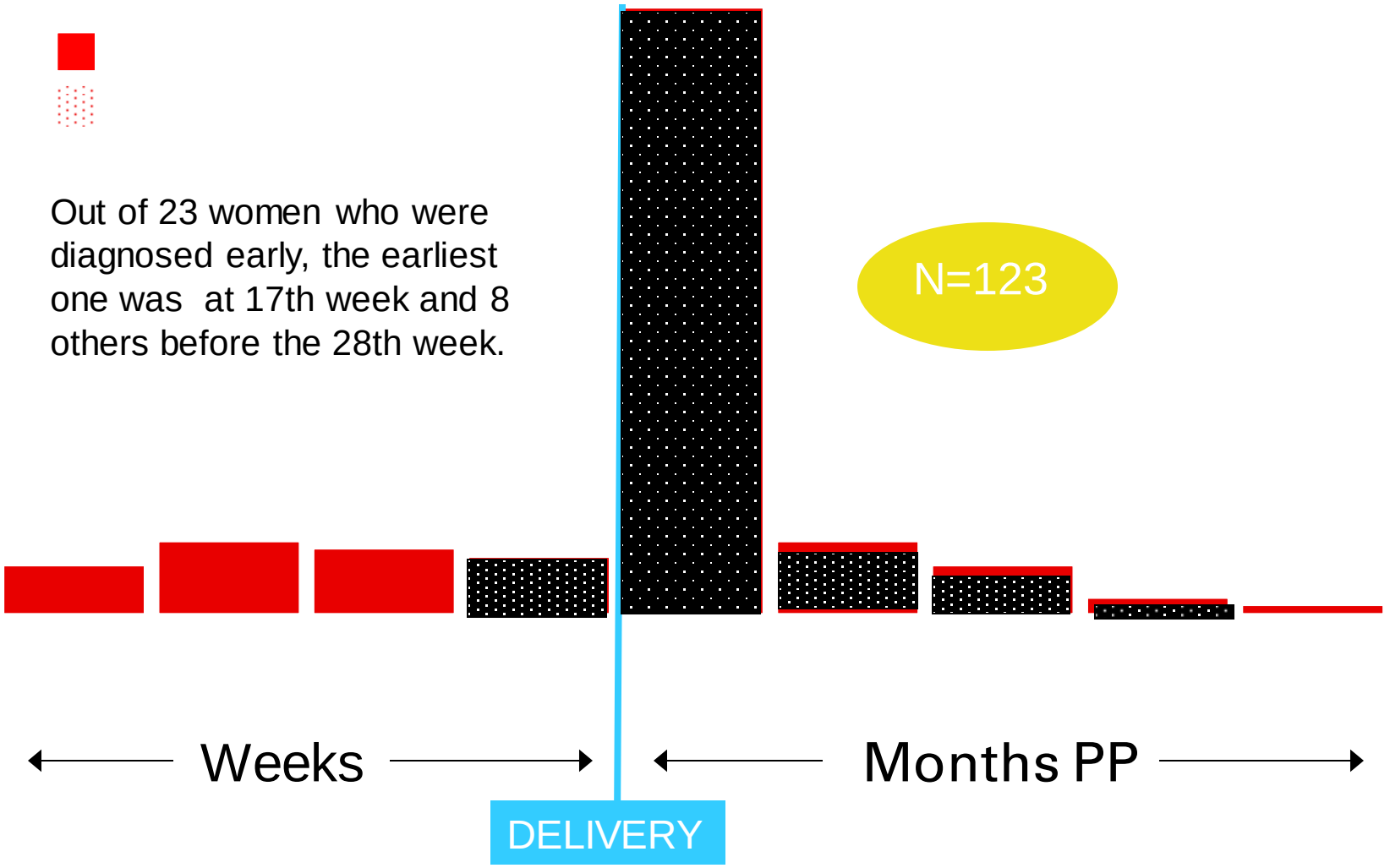
Peripartum Cardiomyopathy
Updated Definition

ESC Working Group. Eur J Heart Failure 2010;12:767

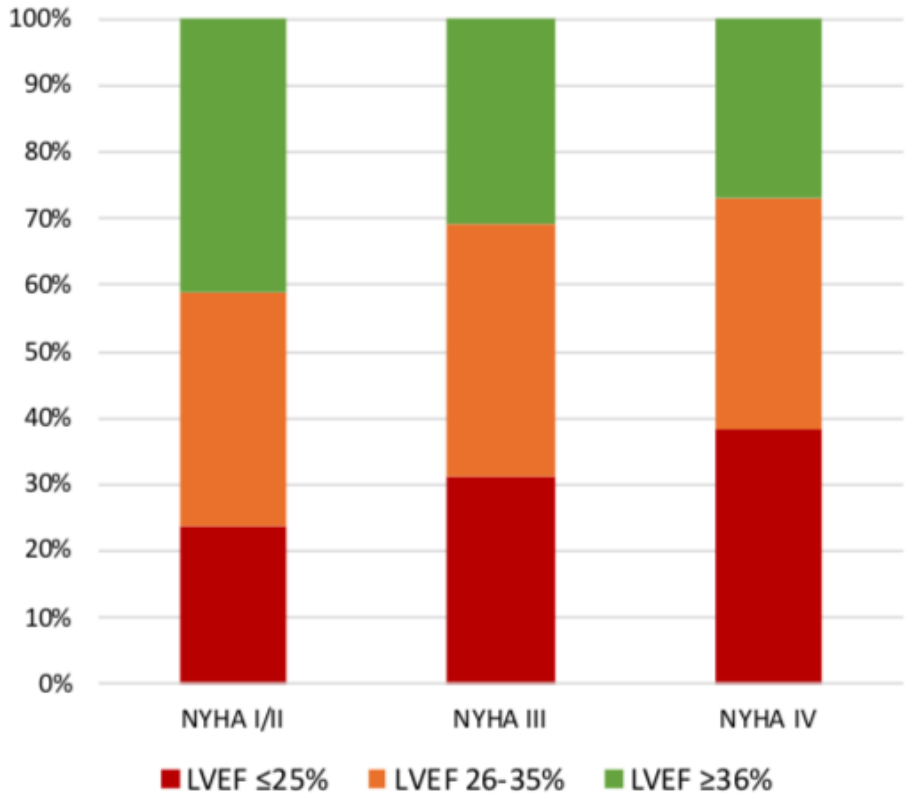
PPCM is an idiopathic cardiomyopathy presenting with HF secondary to LV systolic dysfunction towards the end of pregnancy or in the months following delivery, where no other cause of HF is found.

PPCM – Time of Diagnosis

Elkayam et al. Circulation 2005;111:2050



Baseline left ventricular ejection fraction according to NYHA class



Mortality in the US

Author	Year	# of Patients	Study Type	Mean F/U	% AA	Mortality
Goland	2009	182	Multicenter Retrospective	19 m	29%	7%
Modi	2009	44	Single center retrospective	24 m	89%	16%
Gunderson	2011	110	Population study retrospective	36 m	29%	2%
Cooper	2012	39	Multicenter Prospective	25 m	39%	0%
Harper	2012	85	Epidemiologic Retrospective	7 y	59%	16%
Pillarisetti	2014	100	2 center Retrospective	33 m	55%	11%
Briasoulis	2015	47	Single center Retrospective	12 m	96%	11%
McNamara	2015	100	Multicenter Prospective	12 m	30%	4%

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6 months mortality in 739 women with PPCM from 49 countries was 6%
70% from heart failure
30% sudden death

Sliwa K et al Eur Heart J in press

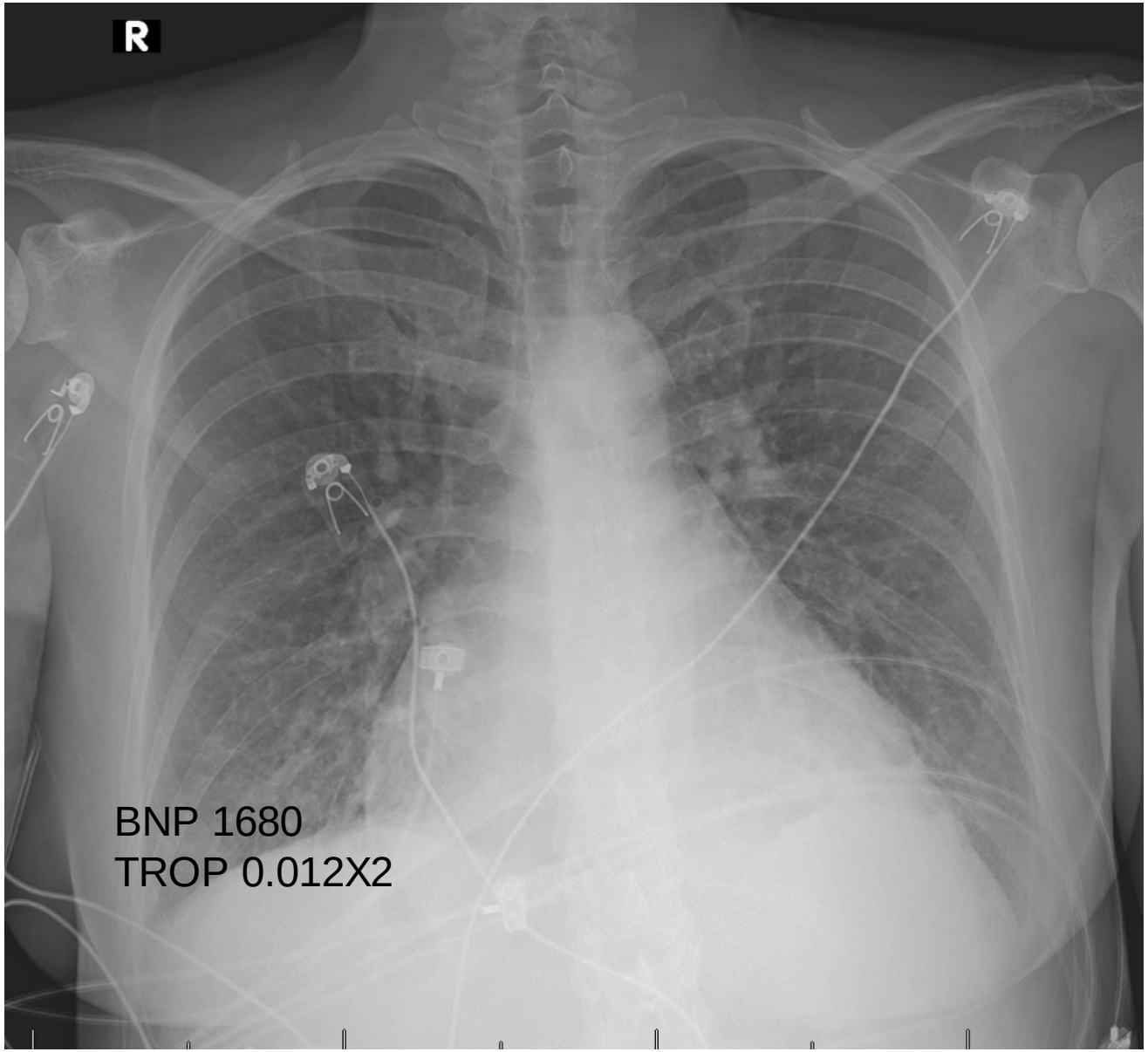
Presentation

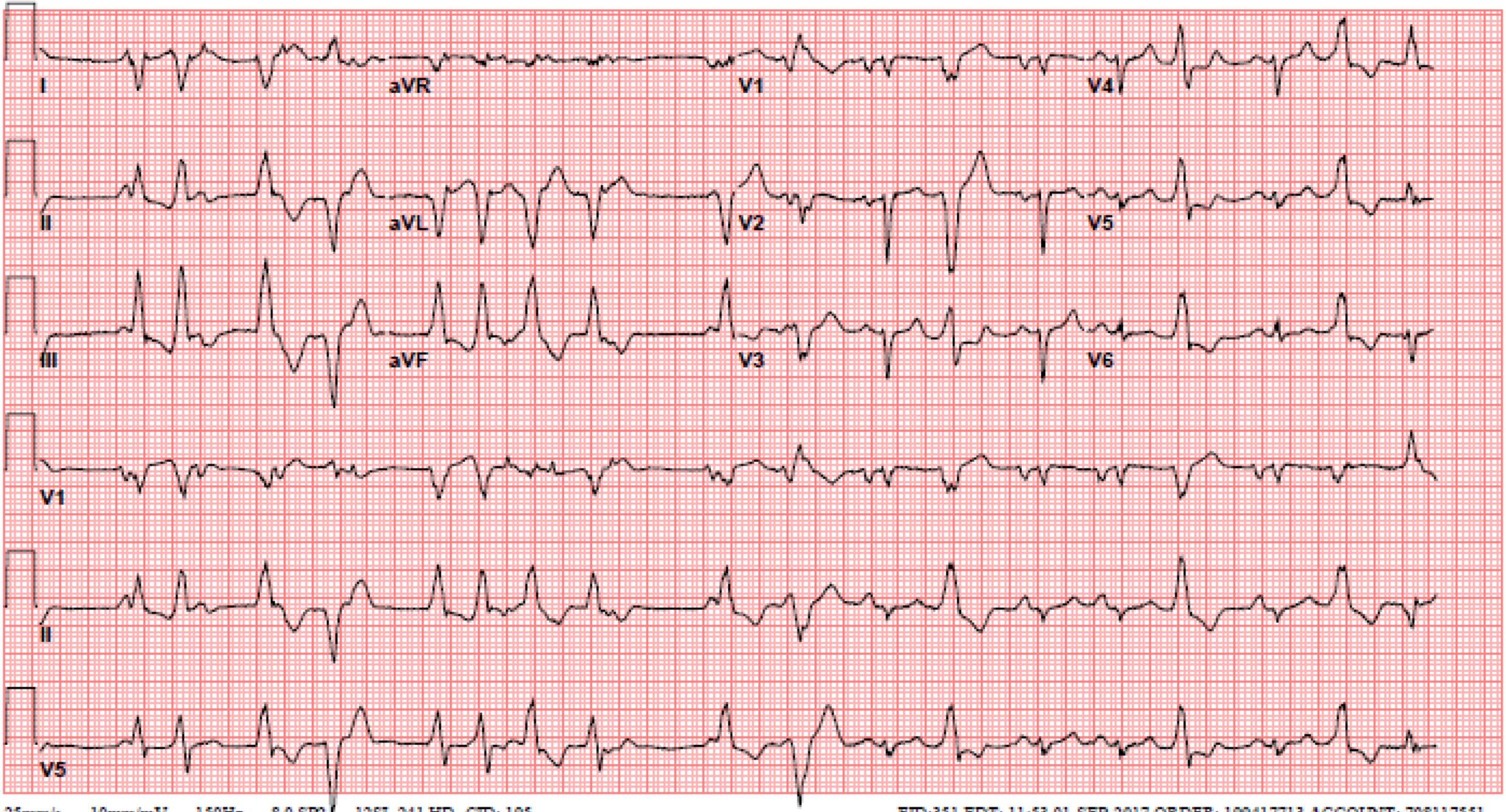
- 30 YO woman G1 P0
- No previous medical history.
- Running half marathon.
- Presented at 26 weeks gestation with progressive exertional edema and palpitations with increasing frequency.
- No toxic habits.

Case

- Vitals: 96/82, P111, RR 25, 92% RA
- Gen: mild distress
- Neck: Supple, JVD 11-12cm
- Irregularly irregular rhythm, 3/6 systolic murmur at apex radiating to axilla
- Lungs: bilateral crackles at bases
- Abd: Soft, gravid
- Ext: Warm, trace edema
- Fetus: No significant compromise.

CXR





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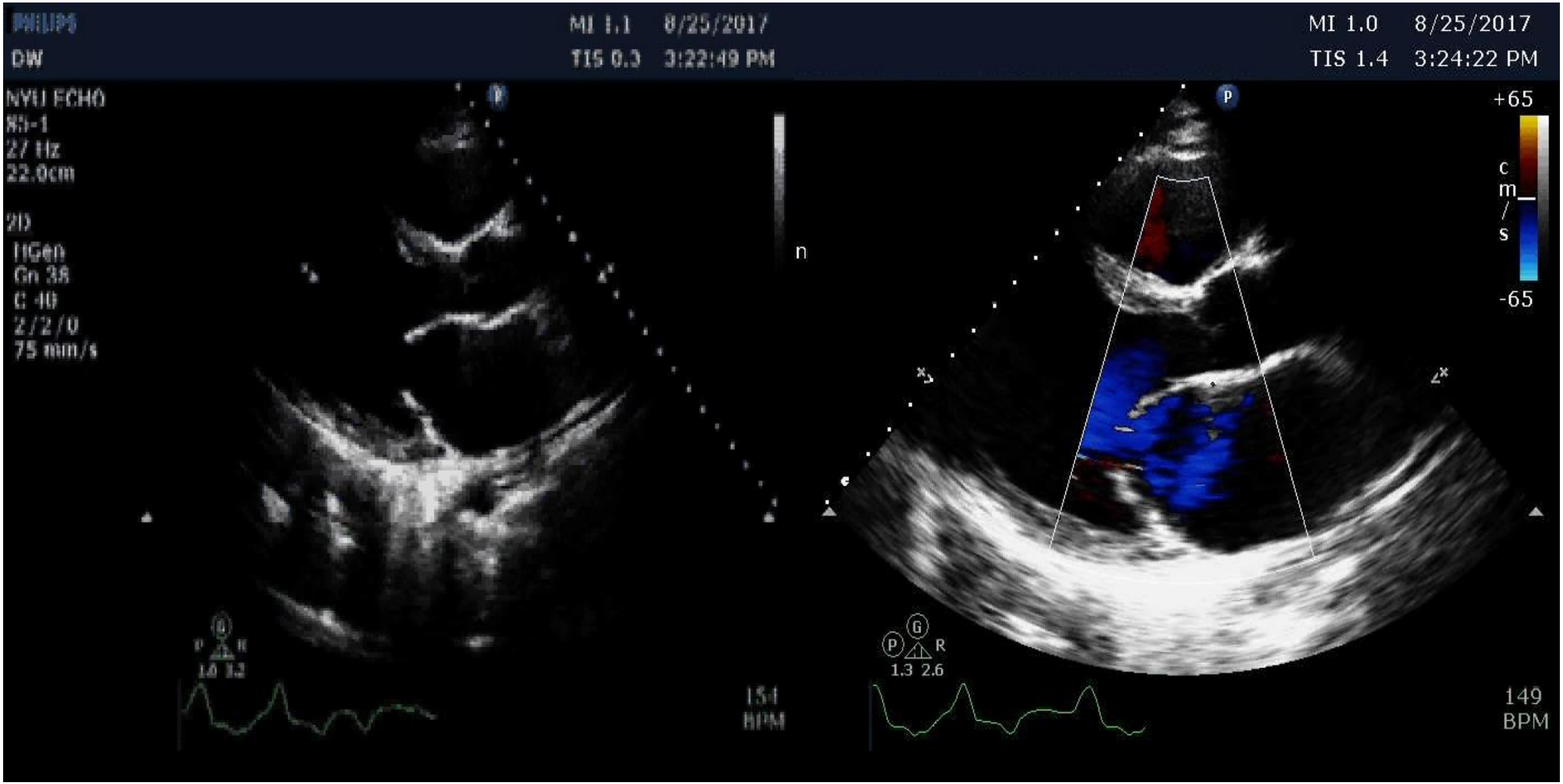
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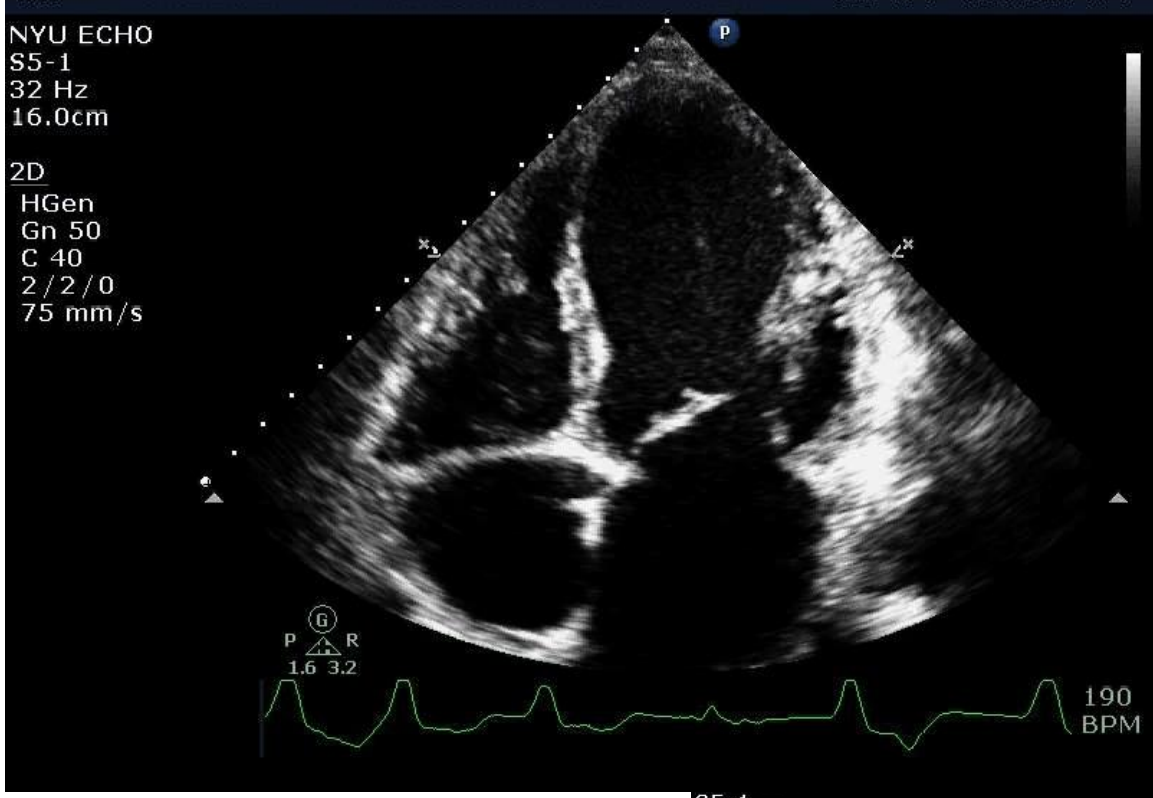
MI 1.1 8/25/2017
TIS 0.3 3:22:49 PM
NYU ECHO
X5-1
27 Hz
22.0cm
2D
HGen
Gn 38
C 40
2/2/0
75 mm/s
1.0 1.3
151
BPM
MI 1.0 8/25/2017
TIS 1.4 3:24:22 PM
+65
cm/s
-65
1.3 2.6
149
BPM


NYU ECHO
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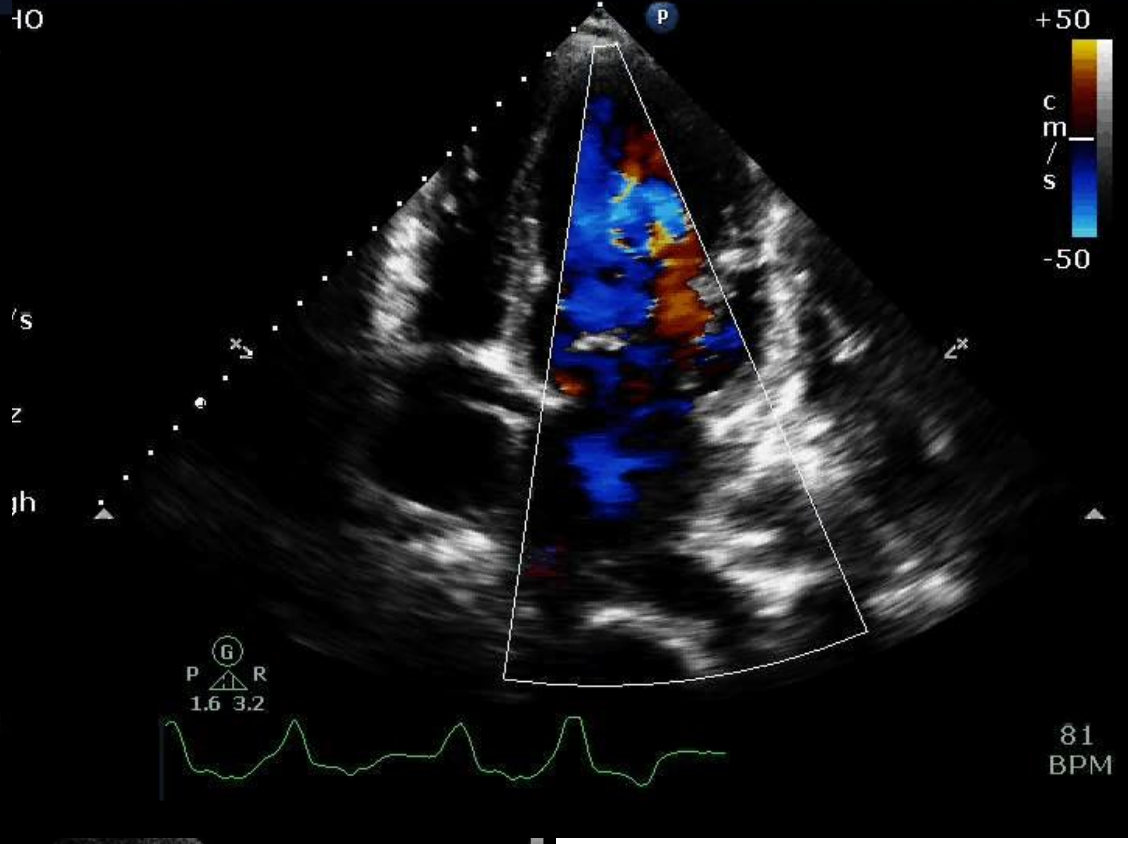
HGen
Gn 50
C 40
2/2/0
75 mm/s
P
P R
1.6 3.2
190
BPM


+50
cm/s
-50
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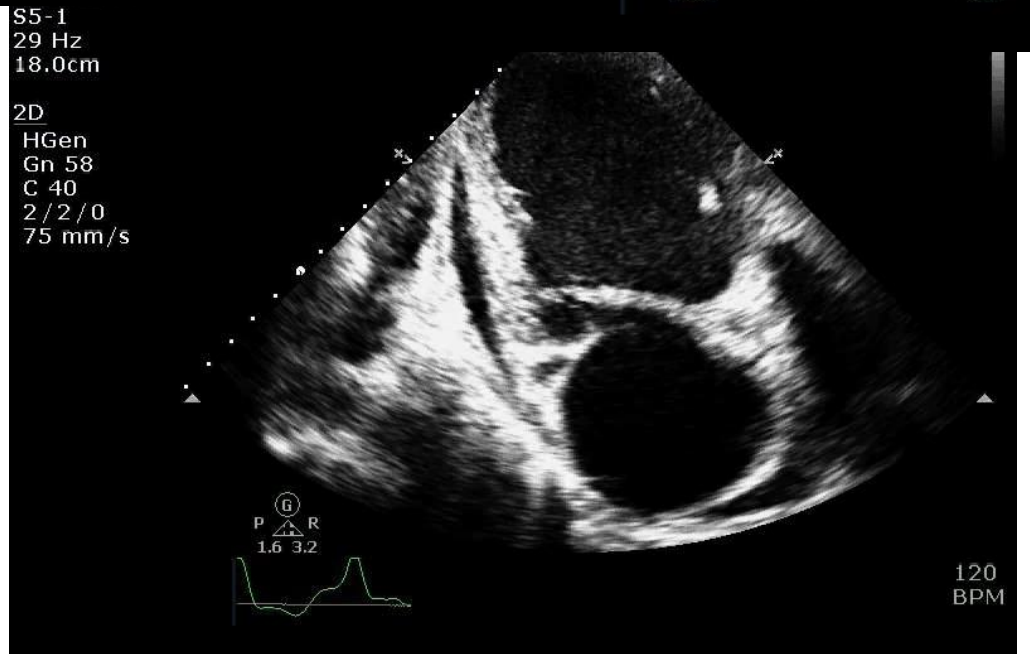
P R
1.6 3.2
81
BPM


S5-1
29 Hz
18.0cm
2D
HGen
Gn 58
C 40
2/2/0
75 mm/s
P R
1.6 3.2
120
BPM

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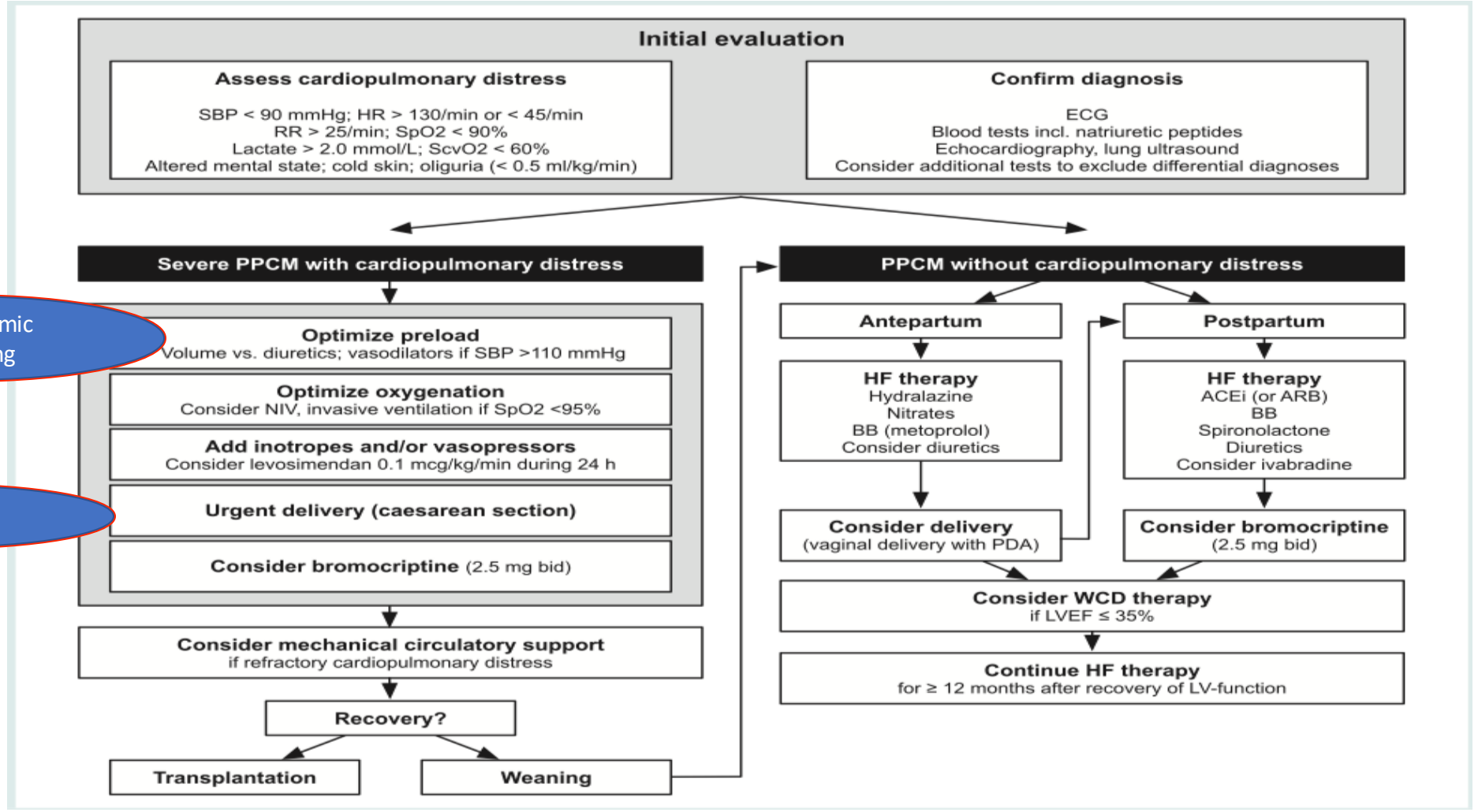


European Journal of Heart Failure 2016; 18, 1096–1105.

Is Dobutamine Unsafe in PPCM?

- Data from the German PPCM registry showed that dobutamine treatment in patients with severe PPCM was associated with an adverse outcome (heart transplantation or LVAD implantation) while almost all patients not receiving dobutamine recovered.

Haghikia A. *Basic Res Cardiol* 2013;108:366

Is Dobutamine Unsafe in PPCM?

- β_1-AR stimulation with isoproterenol in STAT3 knockout mice induced severe cardiac dysfunction and high mortality.
- β_1-AR stimulation impaired glucose uptake and subsequently induced energy depletion, oxidative stress, dysfunction, and death.

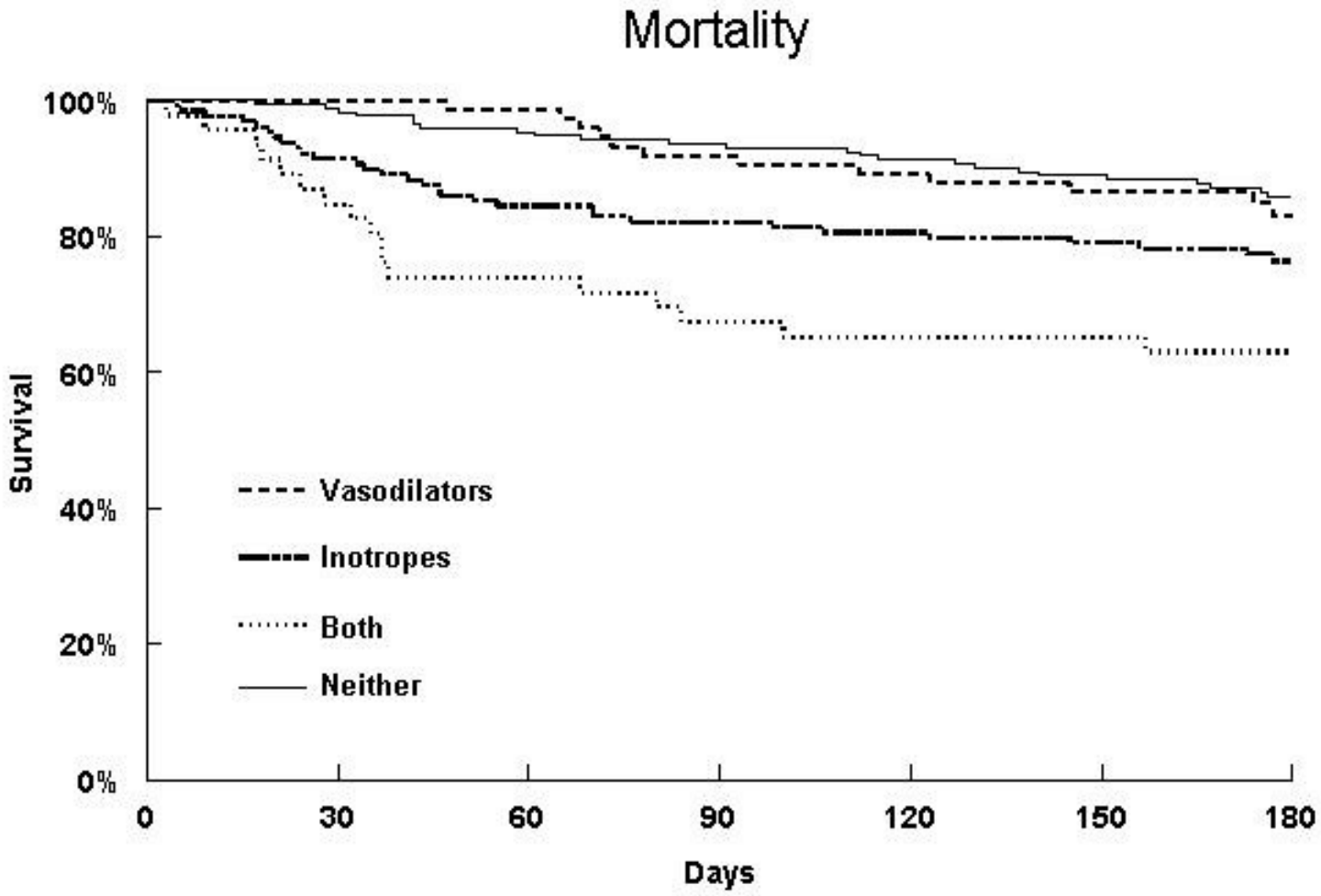
Low STAT3 expression sensitizes to toxic effects of β-adrenergic receptor stimulation in peripartum cardiomyopathy
Staple B et al Eur Heart J 2017;38:349-361

Management of CS complicating myocardial infarction: an update 2019

Thiele H et al European Heart Journal (2019) 0, 1–15

- These drugs increase myocardial oxygen consumption and vasoconstriction which may impair microcirculation and increase afterload. Therefore, any catecholamine should be administered at the lowest possible dose and the shortest possible time.

The ESCAPE Trial:
Use of Inotropes and Vasodilators



Elkayam U et al. *Am Heart J.* 2007;153:98-104.

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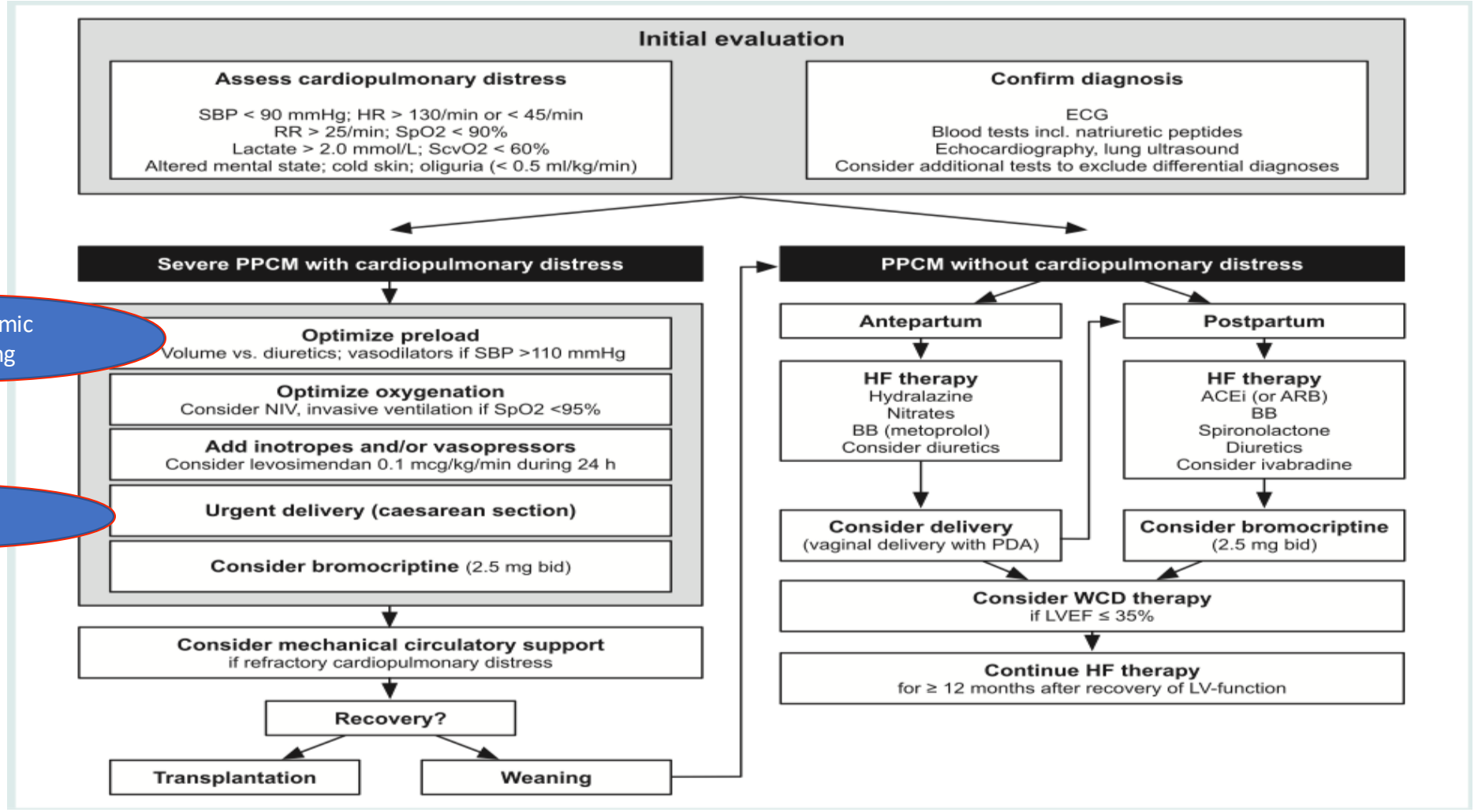

European Journal of Heart Failure 2016; 18, 1096–1105.

Effect of severe prematurity on newborn outcome

N Engl J Med 2019;381:1434-43.

Table 2. Primary and Secondary Outcomes at 24 Months of Age, Corrected for Gestational Age.*

Outcome	Faster Increment: 30 ml/kg/day (N=1394)	Slower Increment: 18 ml/kg/day (N=1399)	Unadjusted Effect Measure (CI)†	Adjusted Effect Measure (CI)†‡
23 wk 0 days to 25 wk 6 days	205 (14.7)	201 (14.4)	0.96 (0.91 to 1.02)	0.96 (0.92 to 1.01)
26 wk 0 days to 27 wk 6 days	291 (20.9)	297 (21.2)	1.01 (0.99 to 1.02)	1.01 (0.99 to 1.03)
28 wk 0 days to 29 wk 6 days	377 (27.0)	383 (27.4)	1.12 (0.98 to 1.28)	1.10 (0.97 to 1.25)
30 wk 0 days to 31 wk 6 days	432 (31.0)	432 (30.9)	1.33 (0.57 to 3.10)	1.28 (0.43 to 3.83)
32 wk 0 days to 36 wk 6 days	88 (6.3)	86 (6.1)	1.45 (0.86 to 2.46)	1.43 (0.79 to 2.57)
			1.49 (0.96 to 2.32)	1.48 (1.02 to 2.14)
			1.08 (0.89 to 1.30)	1.06 (0.89 to 1.27)

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Outcome	Faster Increment: 30 ml/kg/day (N=1394)	Slower Increment: 18 ml/kg/day (N=1399)	Unadjusted Effect Measure (CI)†	Adjusted Effect Measure (CI)†‡
Primary outcome				
Survival without moderate or severe neurodevelopmental disability — no./total no. (%)§¶	802/1224 (65.5)	848/1246 (68.1)	0.96 (0.91 to 1.02)	0.96 (0.92 to 1.01)
Survival — no. (%)	1326 (95.1)	1322 (94.5)	1.01 (0.99 to 1.02)	1.01 (0.99 to 1.03)
Moderate or severe neurodevelopmental disability — no./total no. (%)	354/1156 (30.6)	321/1169 (27.5)	1.12 (0.98 to 1.28)	1.10 (0.97 to 1.25)
Secondary outcomes				
Moderate or severe visual impairment — no./total no. (%)	21/1156 (1.8)	16/1171 (1.4)	1.33 (0.57 to 3.10)	1.28 (0.43 to 3.83)
Moderate or severe hearing impairment — no./total no. (%)	58/1143 (5.1)	41/1172 (3.5)	1.45 (0.86 to 2.46)	1.43 (0.79 to 2.57)
Moderate or severe motor impairment — no./total no. (%)	87/1164 (7.5)	59/1177 (5.0)	1.49 (0.96 to 2.32)	1.48 (1.02 to 2.14)
Moderate or severe cognitive impairment — no./total no. (%)	307/1156 (26.6)	289/1170 (24.7)	1.08 (0.89 to 1.30)	1.06 (0.89 to 1.27)

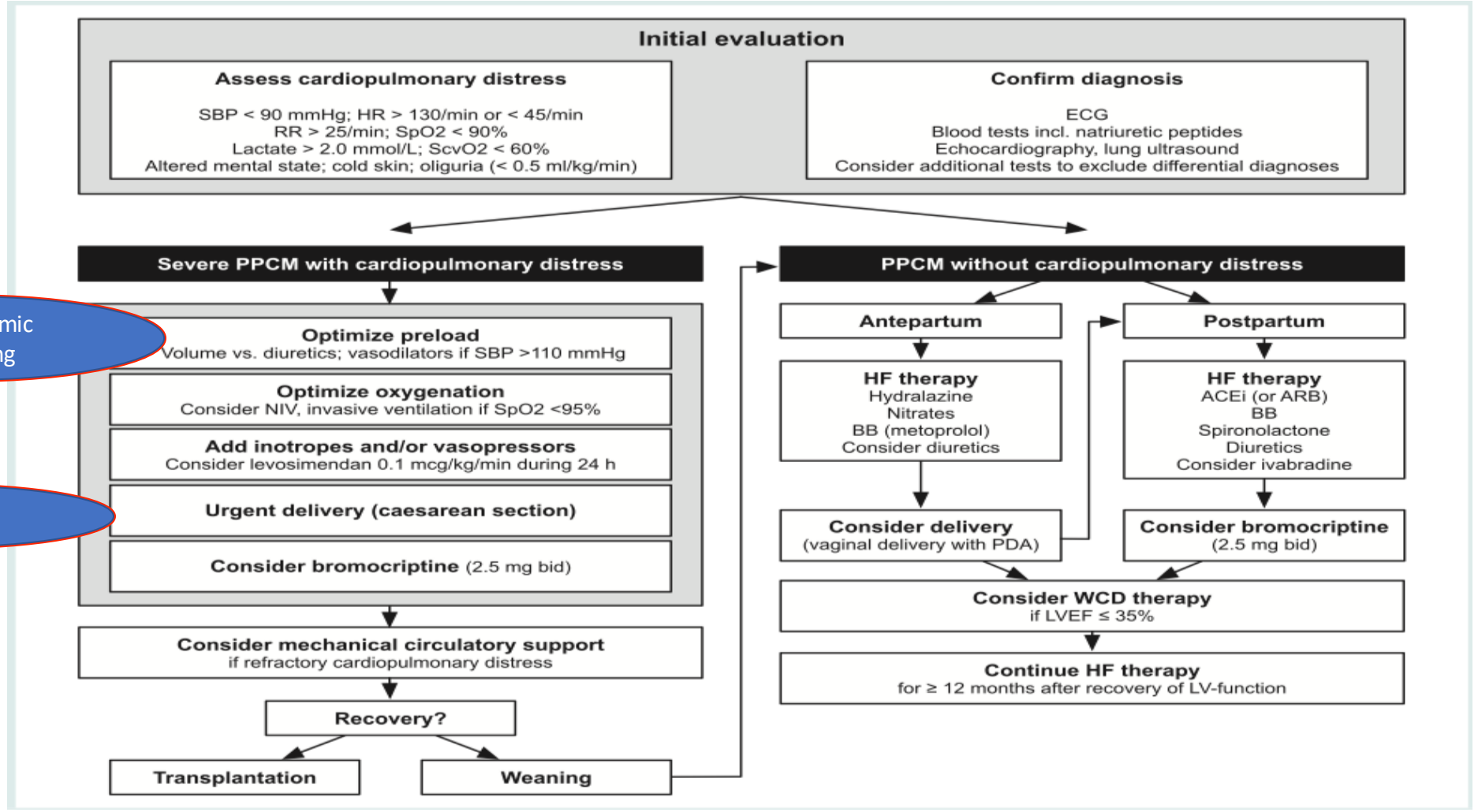
Effect of severe prematurity on newborn outcome

Rysavy MA et al NEJM 2015:372:1801

Table 2. Crude Outcomes by Gestational Age at Birth.*

Outcome	All Infants		Infants Who Received Active Treatment	
	Overall Rate†	Hospital Rate‡	Overall Rate†	Hospital Rate‡
	mean (95% CI)	*median (interquartile range)*	*mean (95% CI)*	*median (interquartile range)*
25 Wk of gestation				
Survival	72.0 (69.4–74.5)	71.2 (65.7–79.5)	72.3 (69.7–74.8)	71.7 (65.7–79.5)
Survival without severe impairment	61.1 (58.3–63.8)	59.3 (54.7–64.3)	61.4 (58.5–64.1)	59.9 (56.2–64.5)
Survival without moderate or severe impairment	44.3 (41.5–47.2)	46.0 (34.9–51.7)	44.5 (41.7–47.4)	46.5 (35.0–51.7)
26 Wk of gestation				
Survival	81.4 (79.2–83.6)	81.0 (78.2–84.0)	81.6 (79.3–83.7)	81.3 (78.9–85.7)
Survival without severe impairment	75.6 (73.2–78.0)	75.7 (69.5–80.0)	75.7 (73.3–78.1)	76.4 (70.8–80.3)
Survival without moderate or severe impairment	58.5 (55.8–61.3)	58.9 (51.6–65.4)	58.6 (55.9–61.4)	59.8 (53.6–67.0)

Heart Failure Association of the European Society of Cardiology Study Group

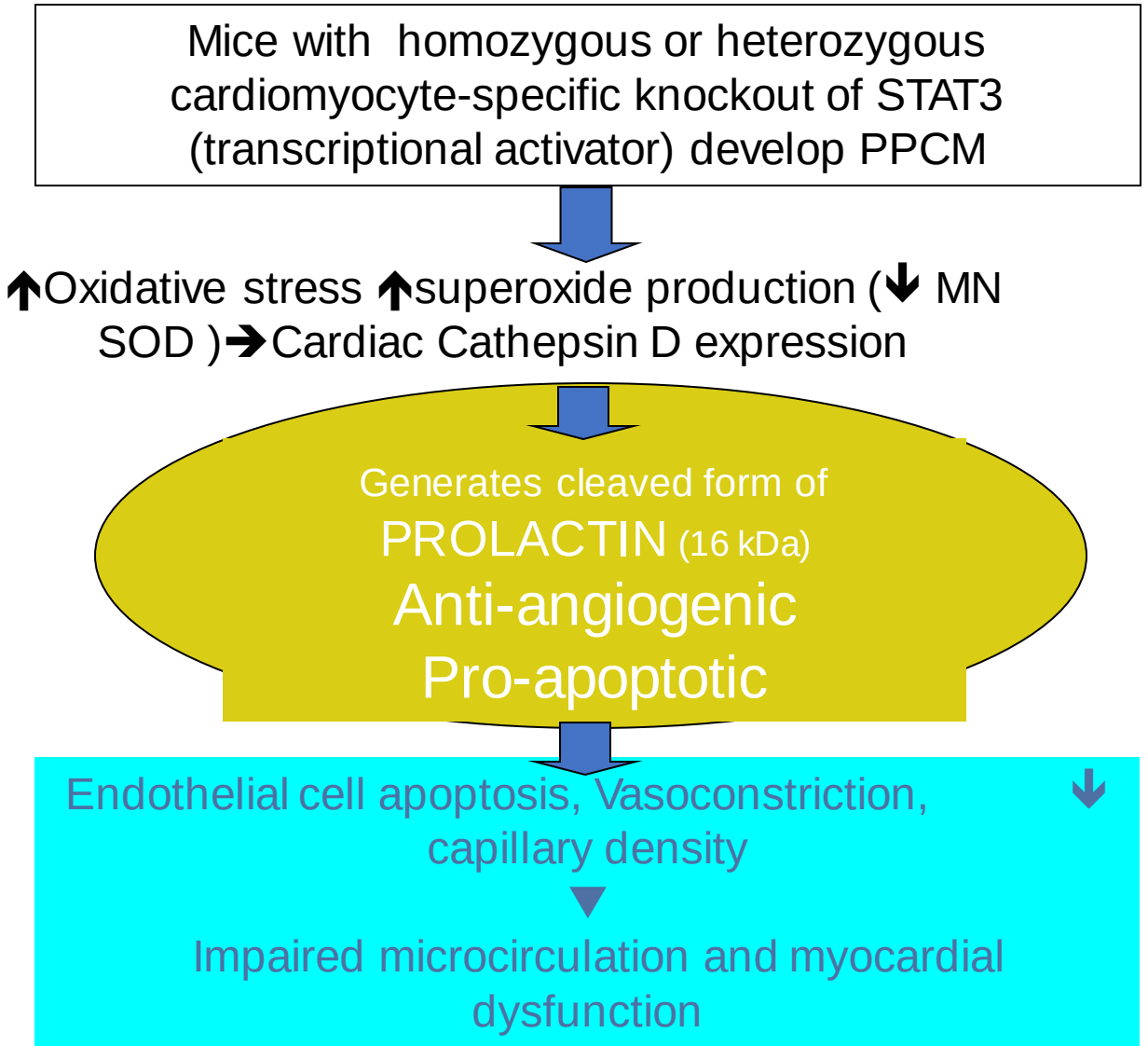


European Journal of Heart Failure 2016; 18, 1096–1105.

PPCM

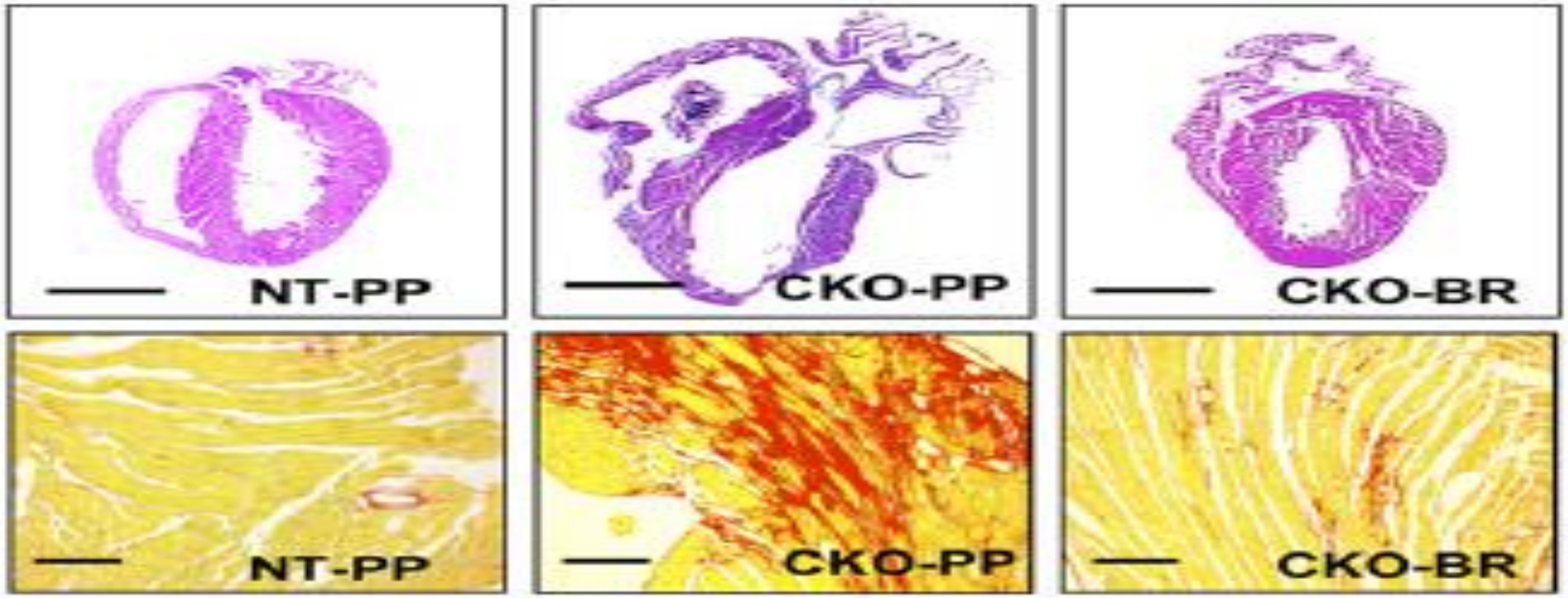
Hilfiker-Kleiner, Drexler et. a.Cell 2007;128:589

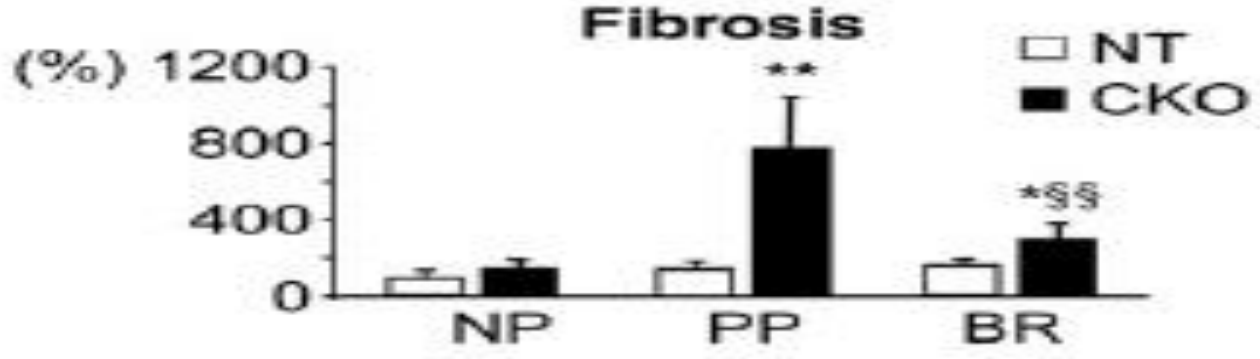
Bromocriptine



A Cathepsin D-Cleaved 16 kDa Prolactin Mediates PPCM

Hilfiker-kliner d et al Cell 2007;128:589





Bromocriptine in PPCM

- Shown to be effective in 2 African studies with phenotypically and probably genetically different PPCM patients.
- German study was inconclusive.
- No information is available in the US.
- No information is available in PPCM + CS.
- Associated with a risk of thromboembolism.
- A strong vasodilator.

The effects of bromocriptine in patients with chronic CHF

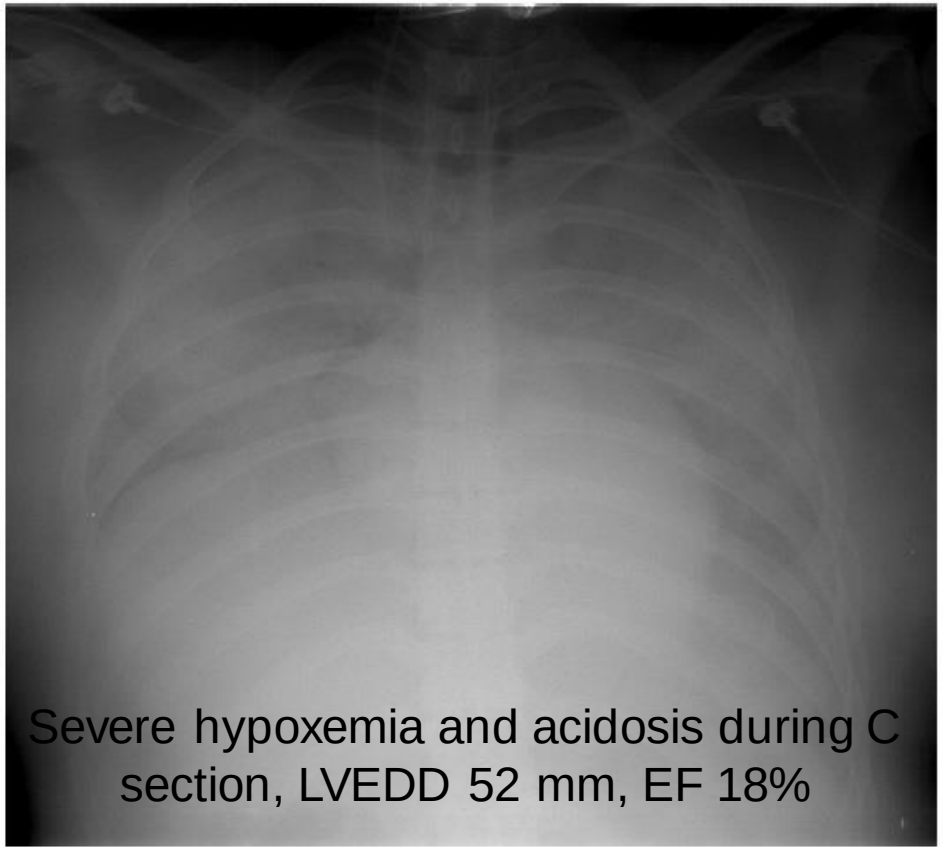
10 patients Bromocriptine 2.5 mg

parameter	Baseline	Bromocriptine
HR (bpm)	87+/-16	78+/-17
SVR (dynes)	1494+/-361	1249+/-289
SVI (ml/m2)	27+/-7	33+/-10
Mean BP (mmHg)	87+/-9	73+/-9
Mean RA (mmHg)	10+/-4	7+/-4
Mean PCW (mmHg)	28+/8	21+/-8

Francis G, Cohn J Am Heart J 1983;106:100-106

Extracorporeal Membrane Oxygenation in a Patient With Peripartum Cardiomyopathy

(Ann Thorac Surg 2007;84:262–4)



Severe hypoxemia and acidosis during C section, LVEDD 52 mm, EF 18%

Fig 1. Severe pulmonary edema was shown in the chest x-ray taken at admission.

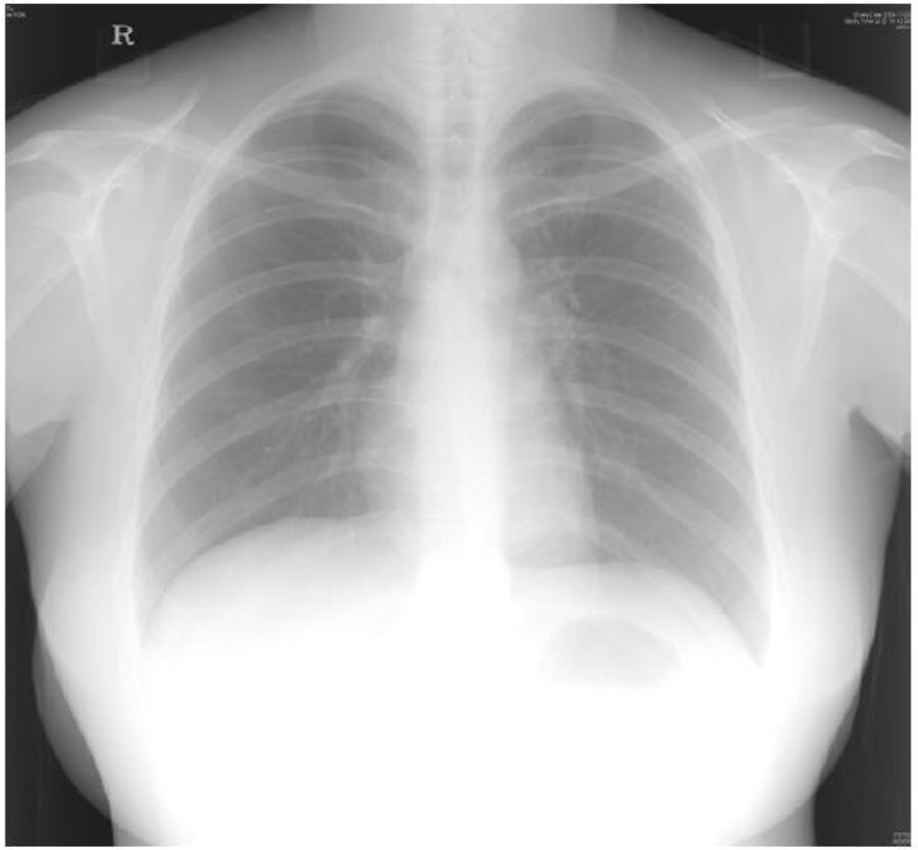


Fig 2. Chest x-ray taken during an outpatient visit (1 month after discharge).

18 YO G1 developed tachycardia and hypertension with severe hypoxemia (PO_2 30%) and acidosis during C section which was not corrected with Inotropic support and 100% oxygen. LVEF 18%. ECMO was use successfully for 24 h, extubated on day 4 and was D/C home on day 12. 1 month after DC LVEDD of 42 mm and LVEF 56%.

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

- A total of 15 women with PPCM supported with Impella devices between November 2008 and October 2015, identified in the global cVAD registry.
- 5 were treated at Hannover medical school and have been reported previously, and the rest of the patients were managed in various US hospitals.
- Median age was 30 years (range 17-39 years)

Elkayam U et al Clinical Cardiol 2019;42:974-81

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

- 8 women (53.3%) were Caucasian 7 AA.
- PPCM was diagnosed post-delivery in 8 , at delivery in 1, and during gestation in 4 women .
- Mean EF of 15 ± 6% and 13 women (87%) presented with CS.

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

- All women were on mechanical ventilation.
- 79% received inotropes/vasopressors.
- 33% were supported with IABP prior to Impella, and 27% received VA ECMO during Impella support

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

During Impella support		
Impella device type		
Impella 2.5	5 (33.3%)	15
Impella CP	8 (53.3%)	15
Impella 5.0	2 (13.3%)	15
Duration of Impella support, hours	265.5 ± 460.6	12
Duration of CS onset to Impella start, hours	15.6 ± 7.7	5
ICU stay, days	34.3 ± 46.7	15
Additional devices implanted/used during Impella support		
IABP	0 (0%)	15
ECMO	4 (26.7%)	15
VAD (CentriMag for RV support)	1 (6.7%)	15

TABLE 4 Comparison of hemodynamics before and on Impella support in women with peripartum cardiomyopathy

Measurements	N	Pre-support	On support	*P*-value
Heart rate, beats/minute	12	113 ± 27	102 ± 29	.35
Mean arterial pressure, mm Hg	11	72 ± 19	91 ± 12	.001
Cardiac index, L/min/m^2	2	2.2 ± 0.2	3.7 ± 0.2	n/a
Cardiac output, L/min	2	4.4 ± 0.0	7.6 ± 1.3	n/a
PCWP, mm Hg	6	32 ± 9	18 ± 9	.01

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

TABLE 5 Adverse events at discharge

Adverse event		N
Death	2 (13.4%)	15
Myocardial infarction	0 (0%)	15
CVA/stroke	0 (0%)	15
Anemia requiring transfusion	3 (20%)	15
Bleeding requiring surgery	0 (0%)	15
Bleeding requiring transfusion	2 (13.4%)	15
Hematoma	0 (0%)	15
Limb Ischemia	1 (6.7%)	15
Vascular complication requiring surgery	1 (6.7%)	15
Vascular complication without surgery	1 (6.7%)	15
Hypotension during support	3 (20%)	15
Device malfunction	1 (6.7%)	15
New renal replacement therapy required	3 (20%)	15
Hemolysis	3 (20%)	15
Thrombocytopenia	1 (6.7%)	15
Infection	3 (20%)	15
Cardiopulmonary resuscitation	1 (6.7%)	15
Ventricular arrhythmia	2 (13.4%)	15
Respiratory dysfunction/failure	1 (6.7%)	15

Use of Impella Heart Pump for Management of Women with Peripartum Cardiogenic Shock

- 2 women (13%) died and 13 (87%) survived to discharge.
- 8 women (53%) had a recovery of native heart function and 6 (40%) were bridged to durable left ventricular assist device (LVAD).

Change in Ejection Fraction

- Among the 11 survivors to discharge with data available, the average LVEF increased from the baseline of 15 ± 7% to 28 ± 18% (P = .04).
- EF at 6 months in 5 patients who were treated medically in addition to Impella support, increased from 11 ± 2% at baseline to 38 ± 17% (P = .01).

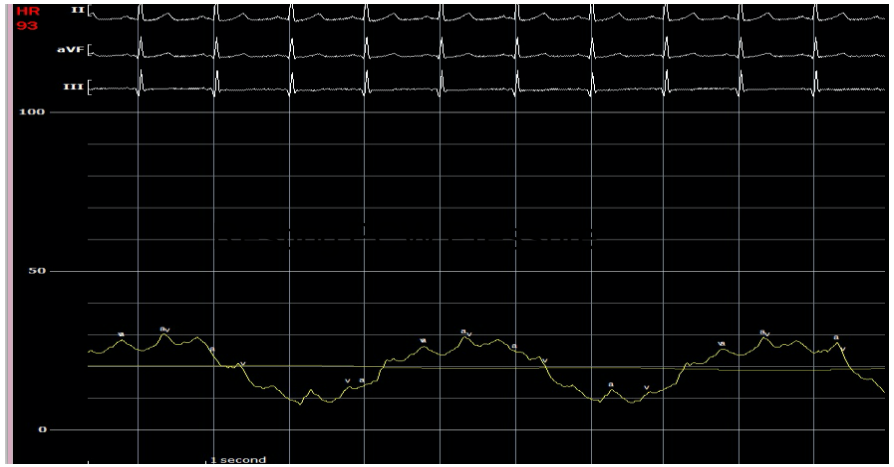
Hospital course

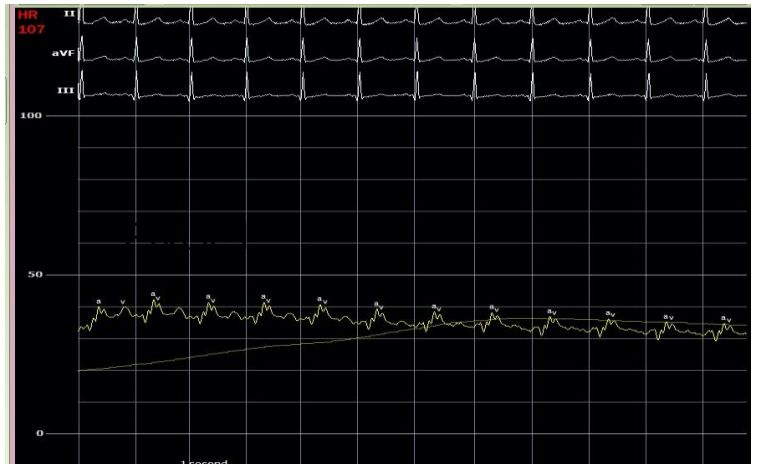
- **Admission (26wks):**
  Esmolol & lidocaine (Mexiletine)
  Unfractionated Heparin
  Furosemide

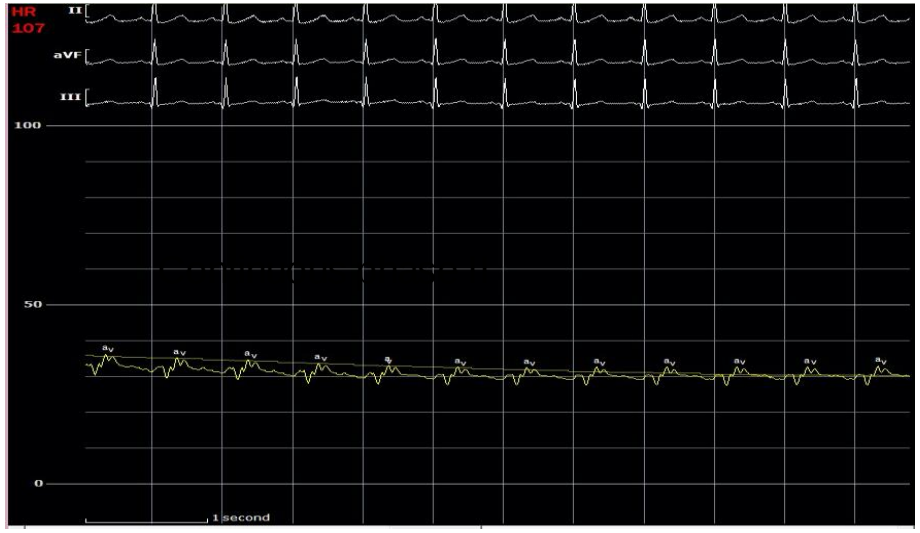
- **Day 3:**
  Improvement of ventricular ectopy frequency
  Trial of Bromocriptine unsuccessful B/O hypotension

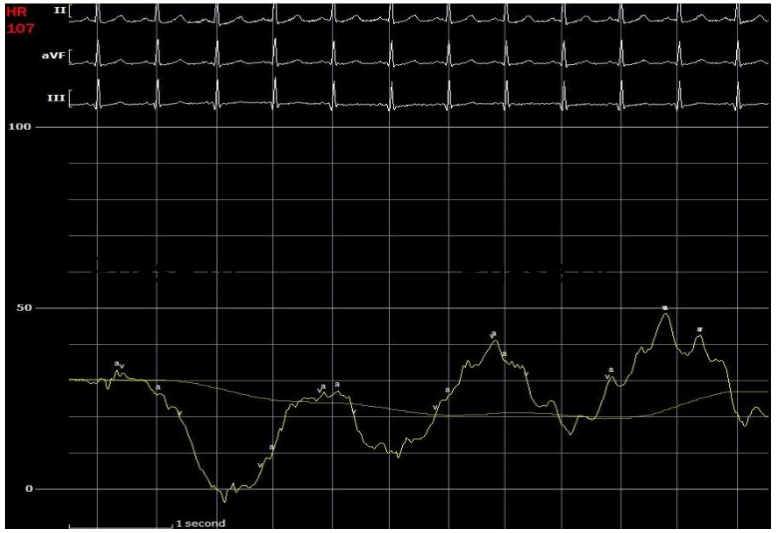
- **Day 12 (27 5/7 wks):**
  PVCs
  BP 90/60s
  PA pressure 60/36 mmHg
  PCWP 35 mmHg
  CO 4, CI 1.9-2.0 L/min/m^2 by FICK

Mitral Stenosis
Hemodynamic Effect of Valsalva

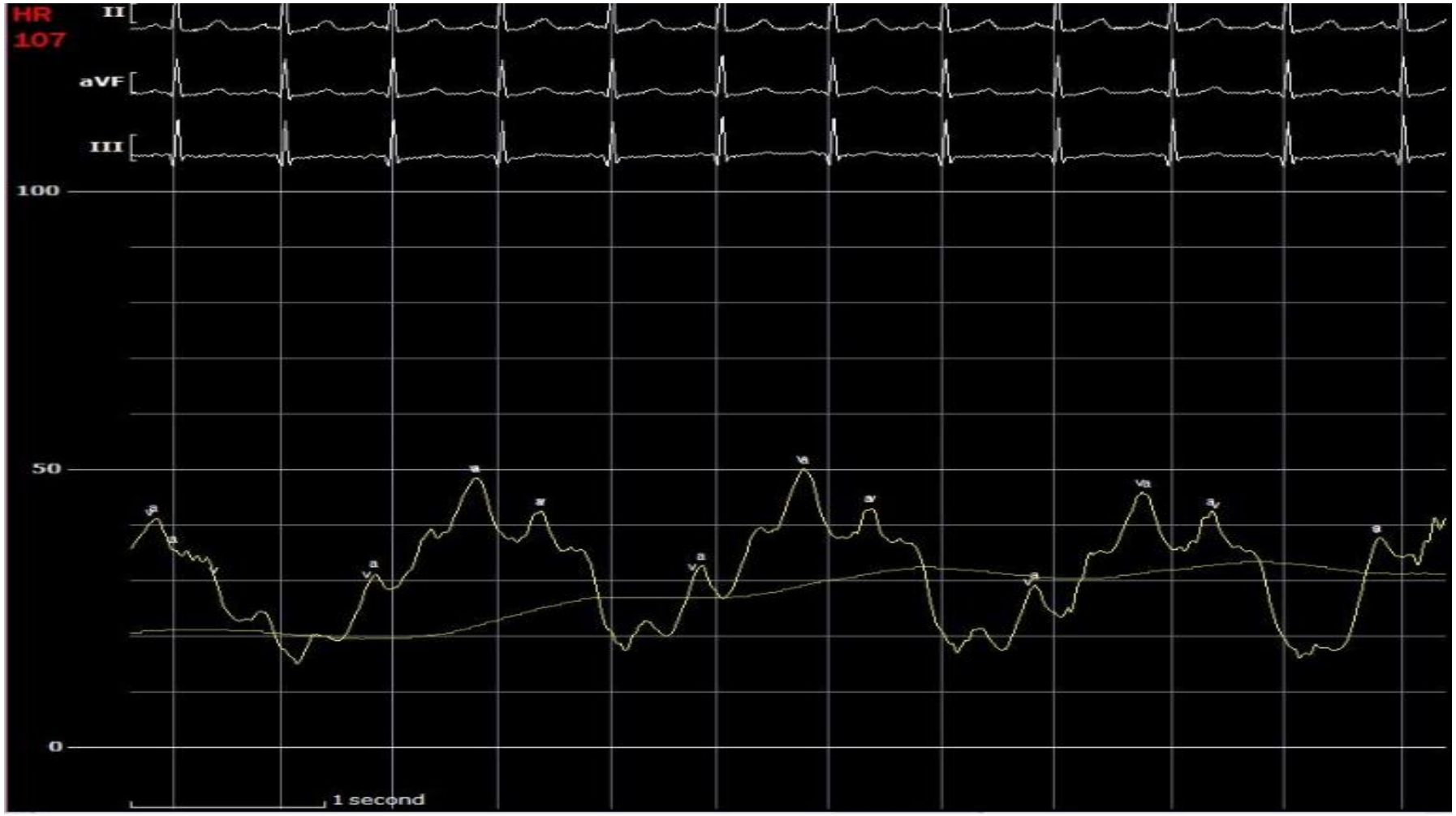








Hemodynamic Effect of Valsalva



Delivery

- Patient was delivered on day 13 at 28 weeks.
- General anesthesia.
- Impella CR placed plus sheat for a potential emergency ECMO.
- Flow 3.5 /l/min, PA 32/16, RA 9.
- C section with left uterine displacement.

Post Delivery

Extubated after several hours

- Impella weaned after 36 hours.
- **Day 15 Heart failure regiment optimized**
- **Bromocriptine x1 wk on UFH**
- **Warfarin**
- **D/C on day 21**
- **Baby pneumothorax and infections D/C home after 3 months.**

Summary

- PPCM can be associated with severe pump failure leading to CS and mortality.
- Presentation during pregnancy is challenging.
- With aggressive therapy including early use of MCS one can delay delivery to allow fetal maturation and bridging patients to either recovery or durable MCS and/or transplantation.

Thank You